

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Perez-Camargo, et al.
Appl. No.: 10/509,951
Conf. No.: 3093
Filed: October 4, 2004
Title: METHOD OF IMPROVING ABSORPTION OF VITAMIN E BY A PET
ANIMAL
Art Unit: 1612
Examiner: Snigdha Maewall
Docket No.: 3714652-509

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I hereby state as follows:

1. My experience and qualifications are as follows:

I am a qualified Veterinarian and registered Member of the Royal College of Veterinary Surgeons in the UK. Since 1994 I hold a Ph.D. by the Department of Applied Biochemistry and Food Science, Nottingham University, UK. During the last 10 years at Nestlé, I had the opportunity to gain research experience about changes in the energy and nutritional requirements of cats and dogs along their different life stages. In particular, changes in their digestive system physiology and intestinal microflora. I also developed several veterinary prescription diets by implementing new research findings and knowledge about the interaction between nutrients and disease in cats and dogs.

2. I am one of the named inventors of the above-identified patent application and am therefore familiar with the invention disclosed therein.

3. Independent Claims 35, 52 and 61 recite, in part, an edible composition comprising a pancreatic function-promoter comprising an acidifier, a liver function-promoter comprising taurine ranging between about 0.1% and about 1% by weight of the edible composition on a dry matter basis, and an intestinal mucosa function-promoter comprising fish oil ranging between about 0.1% and 20% by weight of the edible composition on a dry matter basis.

4. Lipid digestion and absorption by the digestive system is a complex process.

There are three major steps involved in lipid digestibility:

- **Pancreatic Lipolysis:** Lipases operate at acidic pH converting fat molecules to molecules that are more easily digested, i.e., from tri-glycerides to mono-glycerides and fatty acids.
- **Hepatic (liver) Micellar Solubilization:** The products of lipolysis are emulsified with bile acids to form micelles. In felines such as domestic cats, bile acids are conjugated with taurine.
- **Intestinal (Jejunal) Absorption:** Micelles (little fat drops) diffuse into the intestinal cell wall, where the lipid binds to proteins and the triglyceride is reformed. Fats are incorporated into lipoproteins. Bile salts are then re-circulated.

5. All these steps are necessary to achieve normal fat digestibility (fat digestibility is defined as the percentage of fat that the animal retains and is not excreted in feces). Previous published studies aiming at improving fat digestibility focus only on the first step of the process (Lipolysis), and provide lipase enzymes or a combination of lipase, amylase and protease enzymes as a solution.

6. Over a period of several years, the inventors studied the digestibility of numerous diets in a significant number of cats ($n > 1000$). The inventors did batteries of digestibility studies on a continuous basis following Association Of American Feed Control Officials ("AAFCO") protocols. The inventors found that one third of cats over the age of 12 years ("old cats") suffer from low fat digestibility, i.e., fat digestibility of less than 80%. This level of incidence has never been reported. Based upon these findings, the inventors formed a panel of old cats with low fat digestibility to research specifically the phenomena of age related reduction in fat digestibility in old cats. The results showed that the extent of the reduction in fat digestibility in old cats is quite extreme, ranging from 30% to 80% fat digestibility. This extent of low fat digestibility in the old cat population has not been previously reported. Based upon these results, the inventors investigated the causes of the reduction in fat digestibility in these old

cats. A review of known causes of low fat digestibility indicated that none of the previously described pathologies appeared to be the causative factor in low fat digestibility in old cats.

7. The inventors performed postmortem examinations in those old cats that suffered natural deaths. The findings showed that there is not a single well defined pathology for every cat with reduced fat digestibility, but generally it appears that a combined and parallel degeneration of more than one part of the digestive system is involved in fat digestibility. The organs involved are the pancreas, the liver, and the small intestinal mucosa.

8. Evidence shows that rather than a defined pathology, reduced fat digestibility is part of the normal ageing process of cats. In our studies, increasing age has been highly correlated with decreasing fat digestibility. This is not to be confused with Exocrine Pancreatic Insufficiency ("EPI"), a rare and specific pathology that involves a lack of pancreatic enzymes. EPI can be reversed by the supplementation of the diet with pancreatic extract or purified lipases. Our studies showed that the supplementation of enzymes (lipases) on its own in the diet does not solve the problem of low fat digestibility in old cats.

9. Fat digestibility is crucial for the aging cat because our research also found that old cats depend heavily on their ability to maintain body weight and body condition to delay frailty. Body weight loss is a predictor of death in old cats. Fat is the nutrient that provides the higher caloric concentration in the diet. Fat is also a carrier for liposoluble vitamins (like vitamin E) and essential fatty acids (like arachidonic acid), which are essential for the cat.

10. The cat, unlike the rat, mouse, man, pig and dog, is a compulsory carnivore known for its peculiarities in nutritional requirements. This makes extrapolation of studies between cats and these species risky and prone to wrong conclusions. The reduction levels we have found of fat digestibility in old cats have not been described in any other species.

11. With age, in a complex system like the gut, several different organs and functions can "go wrong" simultaneously and in slow progression, leading to a decreased efficiency

manifested in the form of reduced fat digestibility. Specific diagnosis for each specific condition is not easily available, and a single cure to fix them all impossible. Routine veterinary examinations for old pets generally include renal function, dental health, heart condition, body weight, endocrine and hepatic function. Digestibility is definitely not included in routine veterinary evaluations due to the long time it takes to conduct the examination; digestibility assessment requires 10 days. During the 10 days the diet of the pet must be consistent and accounted for, and during the last 5 days the feces need to be collected and analyzed. Further, the symptomatic presentation of several pathologies of the digestive system can be very similar, making the diagnosis difficult. Even when low fat digestibility is diagnosed, the real etiology of the problem cannot be easily determined.

12. To determine if there was an improvement in fat digestibility in old cats fed different diets containing combinations of pancreatic function promoters, liver function promoters, and intestinal mucosa function promoters, a "wet" diet (Diet A), a "dry" diet, (Diet B), a diet containing a pancreatic function promoter (Diet A + citric acid), a liver function promoter (Diet A + taurine), an intestinal mucosa function promoter (Diet A + fish oil in the form of omega 3 oils), and a combination of the promoters (Diet C) were formulated and fed to cats using the procedure given in Example 1 of the above-identified patent application. The citric acid in the diets was in an amount of approximately 0.1% by weight. The taurine in the diets was in an amount of approximately 0.8% by weight. The fish oil in the diets was in an amount of approximately 3% by weight. The results are shown in the attached Figure 1.

13. Referring to Figure 1, the control diets (Diet A and Diet B) showed a fat digestibility of about 61% and 63% respectively. There was no significant difference between fat digestibility of a wet diet and a dry diet. This confirms that the digestibility of wet and dry diets is substantially the same and that diet is not a factor in evaluating digestibility. Diet A + citric acid, Diet A + taurine, and Diet A + fish oil showed an increase in fat digestibility of 6.6%, 6.1% and 5.5% respectively when compared to the control diets. However, surprisingly, the combination of the three promoters showed a much more pronounced affect on fat digestibility. The combination (Diet C) showed an increase in fat digestibility of 17.5%.

14. In old cats with reduced fat digestibility (<80%), the presence of a single pancreatic function promoter (acidifier), a single liver function promoter (taurine), or a single intestinal mucosa function promoter (omega 3 oils) improved the level of fat digestibility (around 5.5 to 6.6%). However, none of these diets increased the level of fat digestibility above 80%, the level considered as normal. When the inventors provided the same old cats with a diet that contains a combination of a pancreatic function promoter (acidifier), a liver function promoter (taurine), and an intestinal mucosa function promoter (omega 3 oils), the improvement in the level of fat digestibility is more dramatic (around 17.5%). See Figure 1. Only with this diet did the old cats reach a level of fat digestibility that was considered normal (above 80%). This is a dramatic effect; not even in young healthy cats can fat digestibility be 100%. Moreover, no digestive system is 100% efficient (every meal produces some fecal content).

15. The results are surprising and unexpected when the percentage of cats that showed an increase in fat digestibility is analyzed as shown in the attached Figure 2. Referring to Figure 2, the percent of cats that had an improved fat digestibility when administered the promoters in combination was 90%, as compared to the 67% to 75% for the promoters alone. This effect is dramatic. About 20% more cats will have increased fat digestibility if administered a combination of promoters than if administered one of the promoters alone. Thus, one critical discovery is that the number of cats that benefit from a combination of a pancreatic function promoter (acidifier), a liver function promoter (taurine), and an intestinal mucosa function promoter (omega 3 oils) is much greater than the number of cats that benefit from a single promoter. Figure 2 shows that 90% of the cats improved their fat digestibility, versus only 75% when fed a diet with a single pancreatic function promoter (acidifier), 67 % with a single liver function promoter (Taurine), or 67% with a single intestinal mucosa function promoter (omega 3 oils).

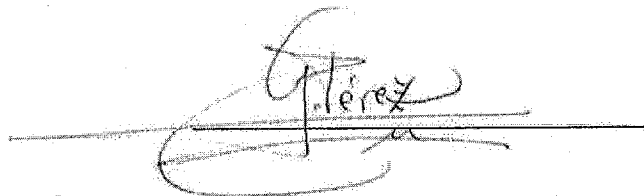
16. As further shown by Figure 1 of the above-identified specification, there is a direct correlation between fat digestibility and enhancement of the serum Vitamin E level. In other words, a composition that increases fat digestibility also increases the absorption capacity

of Vitamin E by the body of the animal. As a result, the combination of the pancreatic function promoter (acidifier), the liver function promoter (taurine), and the intestinal mucosa function promoter (omega 3 oils) that increased fat digestibility in the cat can also increase the absorption capacity of Vitamin E by the cat.

17. In conclusion, the decrease in fat digestibility in old cats is a complex problem that involves a decrease in pancreatic function, liver function, and/or intestinal mucosal function. In most cases, as is frequent with old age, there is not a clear and consistent malfunction, but a concomitant and interrupted decrease of multiple organ efficiency or malfunction. The inventors made a critical discovery in that the number of cats that benefit from an edible composition including a combination of a pancreatic function promoter (acidifier), a liver function promoter (taurine), and an intestinal mucosa function promoter (omega 3 oils) is much greater than the number of cats that benefit from a single promoter. The beneficial effects of the edible composition lead to an increase in fat digestibility in the cat that also correlates to an increase in the absorption capacity of Vitamin E by the cat.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18, United States Code, and that willful false statements may jeopardize the validity of this patent and any patent issuing therefrom.

Date: April 5, 2010

A handwritten signature in black ink, appearing to read "Gerardo Perez-Camargo", is written over a horizontal line. The signature is stylized with a large, sweeping initial "G".

Name: Gerardo Perez-Camargo

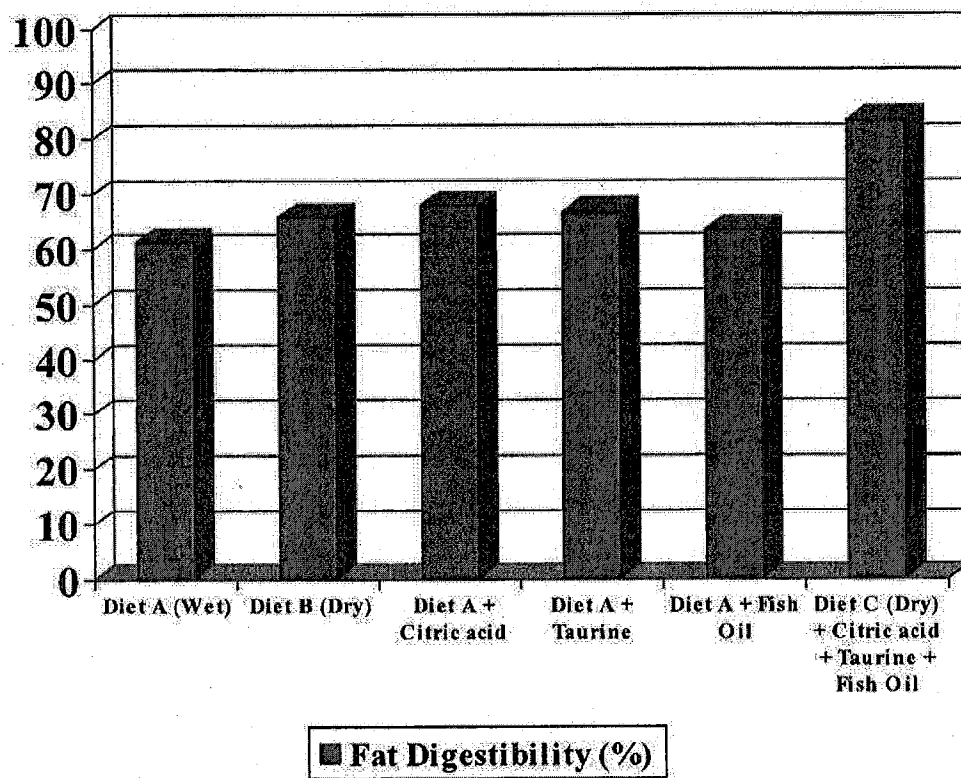


FIG. 1

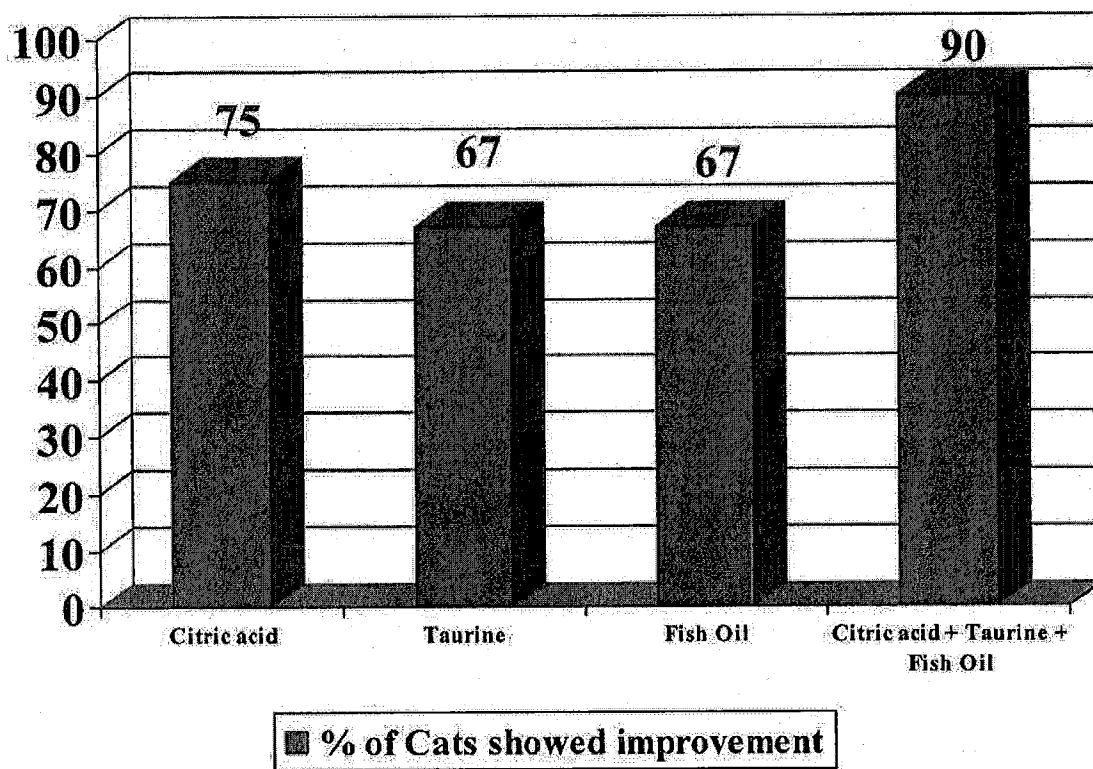


FIG. 2